Remarks

Application Status and Disposition of Claims

Claims 1-36 are pending. Claims 4, 7, 10, 11 and 18 (in part) are under consideration. Claims 1-3, 5-6, 8-9, 12-17, and 19-36 are withdrawn.

Priority under 35 U.S.C. § 119

Applicants thank the Examiner for acknowledging Applicants' claim of foreign priority.

With respect to the Examiner's comments on the entitlement to foreign priority, Applicants wish to point out that their entitlement to priority is a formal matter, and depends solely upon whether the priority requirements under 35 U.S.C. § 119 have been satisfied. It does not require that the Examiner review the foreign priority document to determine whether it sufficiently discloses the subject matter of any claim. Accordingly, the Examiner's comments regarding its disclosure are not relevant to the formal claim of priority and its acknowledgement by the Office.

The Examiner also indicates that because a certified English translation of PCT/JP2004/018437 has not been received, the instant application filing date is April 12, 2007. In response, Applicants respectfully note that MPEP 1893.03(b) explains that the filing date of a U.S. national stage application filed under 35 U.S.C. § 371 is the international filing date, provided that the 35 U.S.C. § 371 filing requirements are met. Accordingly, if the Examiner maintains this position, Applicants respectfully request that he explain how the requirements of 35 U.S.C. § 371 have not been met (and how the Patent Office erred in issuing the Notice of Acceptance) in the present application. In this regard, Applicants note that a translation of the international application is on file in the present application.

Applicants submit that the Examiner is mistaken in his understanding of the requirements of an application filed under 35 U.S.C. § 371, which Applicants submit have been met. The effective filing date of the present application is the international filing date, December 3, 2004. No additional papers or translations are required to establish Applicants' entitlement to that date.

Finally, with regard to the Examiner's comments about the lack of certified translations of the Japanese foreign priority documents, Applicants note that there is no requirement for translations to satisfy the formal claim of priority. The priority claim has been properly made and the Examiner has not raised any issue that would properly call into question whether the formal claim is proper. (Applicants acknowledge that whether a particular claim is supported by a priority document may be relevant in the context of an art-based rejection over intervening art. However, that issue may properly be raised by the Office by making the rejection over the intervening art and allowing Applicants to respond by providing translations, if desired.)

Claim Rejections – 35 U.S.C. § 112, first paragraph

The Office Action maintains the rejection of claims 4, 7, 10, 11, and 18 under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. In particular, the Action states that recitation of the term "comprising" allows for additional mutations or changes in amino acids or nucleotides, and thus the claims are not limited to "1 to 20" amino acid changes or "1 to 60" nucleotide changes as recited.

In response, Applicants have amended the claims to clarify the language noted by the Examiner in the Action. Applicants submit that the amendment clarifies the claims and respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 102

The Office Action maintains the rejection of claims 4, 7, 10, 11, and 18 under 35 U.S.C. §102(b) as allegedly anticipated by Timms-Wilson et al. (*Journal of Microbiological Methods* **46**:77-80, 2001).

In response, Applicants respectfully submit note that the claims have been amended to address the lack of clarity regarding the deletions, substitutions, and/or additions, which prompted the rejection under 35 U.S.C. § 112, first paragraph, discussed above. Applicants respectfully submit that the claims are not anticipated by Timms-Wilson et al. and respectfully request withdrawal of the rejection.

The Office Action also rejects claims 4, 7, 10, 11 and 18 under 35 U.S.C. §102(b), or, in the alternative, under 102(a), as allegedly anticipated by Karasawa et al. (*Biochem J.* **381**:307-312, 2004).

In response, as explained above, the effective filing date of the present application is December 3, 2004. As Karasawa et al. was published in 2004, it cannot qualify as a reference under 35 U.S.C. § 102(b). Applicants further note that Karasawa et al. was published after the filing date of Applicants' foreign priority applications, JP2003-404472 and JP2004-018344, verified translations of which are provided herewith. Applicants invite the Examiner to review the attached translations and determine their effect on the rejection over Karasawa et al.

Obviousness-Type Double Patenting

The Office Action rejects claims 4, 7, 10, 11, and 18 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-8 of U.S. Patent No. 7,541,451. The Office Action also rejects claims 4, 7, 10, 11, and 18 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-8 of U.S. Patent No. 7,226,993.

Initially, it appears that this rejection is based on the Examiner's understanding of the prior claims, which would have allowed for a greater number of deletions, substitutions, or additions, than specifically claimed. To the extent that the rejection was based on this interpretation, Applicants submit that the present amendments clarify that issue and accordingly, overcome the rejection. However, to the extent that the present amendments do not address the Examiner's concerns, Applicants provide the following comments.

The Examiner notes that the "polypeptide has to form monomer before become multimer." However, the protein mKO of the present invention emits fluorescence in the form of a monomer, and mKO is present only in the form of a monomer. On the other hand, the protein KO of U.S. Patent No. 7,226,993 emits fluorescence in the form of a multimer.

Applicants provide herewith an experiment and results (attached hereto) in which each fluorescent protein was produced in *E. coli* and the lysate of the *E. coli* was subjected to electrophoresis for detection of fluorescence. As shown in the results, only a band corresponding

to a dimer was observed for the KO protein. Namely , KO does not emit fluorescence in the form of a monomer. On the other hand, a band corresponding to a monomer was observed for the mKO protein.

As to the KCy protein of U.S. Patent No. 7,541,451, only a band corresponding to a dimer was observed. Thus, KCy does not emit fluorescence in the form of a monomer.

As noted above, KO and KCy have a property of forming a multimer, and emit fluorescence only in the form of a multimer. For a fluorescent protein which is used as a tag, or label, formation of a multimer is disadvantageous for the purpose of analysis of another analyte to which the fluorescent protein was fused. For example, when a fluorescent protein such as KO or KCy, which forms the dimer, is used a tag or label for an analyte that forms a trimer and shows its function, the function of the analyte is inhibited and analysis of interest cannot be performed.

The protein mKO of the present invention emits fluorescence in the form of a monomer. Thus, the molecular weight as a tag can be small and mKO can be applied to targeting to subcellular organelle as discussed further below.

The specification discloses Example 4 as follows:

> Example 4: Targeting to mitochondria
>
> 12 amino acids (MLSLRQSIRFFK) at the N-terminus of cytochrome oxidase subunit 4 derived from yeast were added to each of the N-termini of KO and mKO. Thereafter, targeting to the mitochondria of HeLa cells was conducted, so as to label the mitochondria. As a result, it was confirmed that KO (dimer) was not exactly targeted to the mitochondria, and that the mitochondria was stained in a granulated state (Figure 4). On the other hand, mKO (monomer) was exactly targeted to the mitochondria, and narrow filamentous mitochondria were observed. Thus, effectiveness obtained by monomerization was confirmed (Figure 5).

In this example, the specification specifically describes how the mKO of the present invention is advantageous for targeting of subcellular organelles, as compared to KO of U.S. Patent No. 7,226,993.

Finally, Applicants note that KCy of U.S. Patent No. 7,541,451 has a fluorescent color that is different from that of the present invention, and the analysis purpose and filter for KCy is different from those of the present invention. Still further, the excitation peak (about 450 nm) of KCy is overlapping with the excitation of endogenous fluorescent component (such as riboflavin) of the cell. Thus, KCy is likely to be sensitive to endogenous fluorescence , while mKO has no such problem and is advantageous.

In view of the foregoing remarks, Applicants respectfully submit that the claims of the present application are not obvious in view of any claims of U.S. Patent No. 7,541,451 or 7,226,993. Applicants respectfully request withdrawal of the rejection.

Conclusion

In view of the foregoing remarks and amendments, Applicants respectfully request withdrawal of the objections and rejections of record and allowance of the claims. If the Examiner has any questions or wishes to discuss this application further, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

The Patent and Trademark Office is hereby authorized to charge Deposit Account No. 19-0089 any fee necessary to ensure consideration of the submitted materials.

Respectfully Submitted,
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Attachments:

Verified English language translation of JP2003-404472
Verified English language translation of JP2004-018344
Brief description of experimental methods and results

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